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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,006	09/14/2005	Patrick Irving Eacho	X-13055	1872

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ELI LILLY & COMPANY
PATENT DIVISION
P.O. BOX 6288
INDIANAPOLIS, IN 46206-6288

EXAMINER	
STOCKTON, LAURA LYNNE	
ART UNIT	**PAPER NUMBER**
1626	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	04/06/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 04/06/2007.

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Office Action Summary	Application No.	Applicant(s)	
	10/550,006	EACHO ET AL.	
	Examiner	Art Unit	
	Laura L. Stockton, Ph.D.	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *September 14, 2005 {Prelim. Amendment}*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1, 3-12, 16 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-12, 16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/14/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-12, 16 and 17 are pending in the application.

Information Disclosure Statement

The Examiner has considered the Information Disclosure Statement filed on September 14, 2005.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-6, 10-12, 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No support was found in the specification or the originally filed claims for the amendments, per the Preliminary Amendment filed September 14, 2005, for:

a) the change in carbon ranges for the substituent "$(C_5$-$C_7)$alkyl", under the definition of R_1 in claims 1 and 3;

b) the added substituent "$(C_3$-$C_4)$alkylaryl" under the definition of R_1 in claim 1; and

c) the number of substitutions on the aryl or heterocyclic rings, under the definition of R_1 in claim 1.

Applicant did not state where {page number(s) and line number(s)} support could be found for this changes nor did Applicant make the statement that no new matter has been added. Applicants should specifically point out the support for any amendments. See M.P.E.P. §§

714.02 and 2163.06. Therefore, the claims lack written description as such.

Claims 10-12, 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,

5. the presence or absence of working examples,

6. the breadth of the claims,

7. the quantity of experimentation needed, and

8. the level of the skill in the art.

The nature of the invention

Applicant is claiming a methods of inhibiting hepatic lipase and/or endothelial lipase activity, treatment or amelioration of diseases or the effects of elevated hepatic lipase and/or endothelial lipase activity comprising a compound of formula (I). From the reading of the specification, it appears that Applicant is asserting that the instant claimed compounds would be useful for the treatment or prevention of diseases such as hypercholesterolemia, hyperlipidemia, stroke, hypertriglyceridemia, atherosclerosis and related diseases..

The state of the prior art and the predictability or lack thereof in the art

The state of the art is that the prevention of diabetes remains highly unpredictable. Colagiuri et al. {American Journal of Public Health, September 2006, Vol. 96, No. 9, pages 1562-1569} state "Type 2 diabetes is a complex metabolic disorder triggered by lifestyle factors superimposed on a genetic predisposition." Colagiuri et al. also state "Although we recognize the benefits of science, surgery, and service delivery in relation to certain aspects of chronic disease prevention, it is clear that, either independently or in concert, none can achieve the broad scale changes required to prevent diabetes and obesity on a population basis."

According to Bruno et al. {Expert Opinion Emerging Drugs, (2005), 10(4), pages 747-771}, diabetes mellitus is a major health problem that affects over 170 million people worldwide. Park {Diabetes Research and Clinical Practice 66S (2004), S33-S35} states current methods of treating diabetes is inadequate and that current

strategies to prevent type 2 diabetes mellitus are based on efforts to reduce insulin resistance and to preserve or increase pancreatic beta cell function in high risk individuals. Park also states, "It appears that multiple genes with weak effect are involved in the development of type 2 diabetes mellitus which makes searching diabetogenic genes more complicated." Further, Choi et al. {Journal of Lipid Research, Volume 43, 2002, pages 1763-1769} indicate that there is some suggestion that endothelial lipase plays a role in the development of atherosclerosis. Choi et al. also state, "However, there is only limited amount of information available about this enzyme" and that more studies are needed. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction or guidance present and the presence or absence of working examples

There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the diseases claimed in the pharmaceutical composition and methods. That a single class of compounds can be used to treat, prevent, ameliorate or inhibit all of the diseases embraced by the claims is an incredible finding for which Applicant has not provided persuasive supporting evidence.

The breadth of the claims

The breadth of the claims is treating, preventing, ameliorating or inhibiting all diseases which are mediated by hepatic lipase and/or endothelial lipase.

The quantity of experimentation needed

The nature of the pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological

activities for each of the diseases instantly claimed in the composition. The quantity of experimentation needed would be undue when faced with the lack of testing, and when faced with the unpredictability of the pharmaceutical art. Thus, factors such as "sufficient working examples", "the level of skill in the art" and predictability, etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims.

The level of the skill in the art

Even though the level of skill in the pharmaceutical art is very high, based on the unpredictable nature of the invention and state of the prior art, one skilled in the art could not use the claimed invention without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-6, 9-12, 16 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the additional comma after "(C_5-C_7)alkyl" under the definition of R_1 makes it appear that something is missing.

In claim 1, under the definition of R_3, R_4, R_5 and R_6, on the possible substitutions on the alkyl, alkenyl, phenyl or aryl groups, an "and" is needed before "(C_1-C_6)haloalkyl".

Claim 3 lacks antecedent basis from claim 1 for R_1 representing:

a) -O-(C_1-C_3 alkyl); and

b) $-CF_3$.

Claim 4 lacks antecedent basis from claim 1 for R_1 representing "benzyl".

Claim 5 lacks antecedent basis from claim 1 for R_3, R_4, R_5 and R_6 representing:

a) (C_1-C_4) alkyl;

b) $-O-(C_1-C_3$ alkyl);

c) (C_5-C_{12})cycloalkyl;

d) COOH; and

e) halo.

Claim 6 lacks antecedent basis from claim 1 for R_5 representing:

a) COOH;

b) chloro; and

c) bromo.

Claim 7 is confusing and should be rewritten. A suggestion for re-writing claim 7 is by deleting "of formula(I)..... wherein R_1 through R_6 are selected to provide a compound".

Claims must, under modern claim practice, stand alone to define an invention, and incorporation into claims by express reference to the specification is not permitted. *Ex parte Fressola*, 27 USPQ 2d 1608 (1993). It is improper for claims to refer to subject matter not contained therein, even if the subject matter is contained in the specification. Therefore, independent claim 9 is indefinite because the claim fails to identify the structure of formula I in the claim.

In claim 10, the purpose for "inhibiting hepatic lipase and/or endothelial lipase activity" has not been stated in the claim {e.g., to treat what?}.

Claim 10 lacks antecedent basis from claim 1 because of the term "prodrug".

In claim 12, one cannot treat and/or ameliorate at the same time. Only one or the other is possible.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. {U.S. Pat. 3,517,022} and Takahashi et al. {JP 48-029134}, each taken alone or in combination with each other.

Determination of the scope and content of the prior art (MPEP §2141.01)

Applicant claims benzisothiazolone compounds. Miller et al. (columns 1-2; column 8, lines 31-34; and especially the compound in column 2, line 43 and the compound in column 5, lines 66-67) and Takahashi et al. (page 1; and especially the second compound listed on

page 2) each teach benzisothiazolone compounds that are structurally similar to the instant claimed compounds.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the compounds of the prior art and the compounds instantly claimed is that the instant claimed compounds are generically described in the prior art.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

The indiscriminate selection of "some" among "many" is *prima facie* obvious, *In re Lemin*, 141 USPQ 814 (1964). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g., fungicidal).

One skilled in the art would thus be motivated to prepare products embraced by the prior art to arrive at the instant claimed products with the expectation of

obtaining additional beneficial products which would be useful in treating, for example, fungicides. Since Miller et al. and Takahashi et al. teach fungicidal benzisothiazolone compounds that are structurally the same as, or similar to, each other, the combination of the prior art references would also teach the instant claimed invention. The instant claimed invention would have been suggested to one skilled in the art and therefore, the instant claimed invention would have been obvious to one skilled in the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:15 am to 2:45 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for

unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

The Official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Laura L. Stockton, Ph.D.
Patent Examiner
Art Unit 1626, Group 1620
Technology Center 1600

March 29, 2007